







## Original Research Article

# One pot synthesis of heterocyclic dihydroquinoline analogs incorporating quinoline and pyrimidine fused rings in condensation reaction using NCTDSS as a catalyst

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TiO<sub>2</sub> nanoparticles

Dihydroquinoline

Michael addition reaction

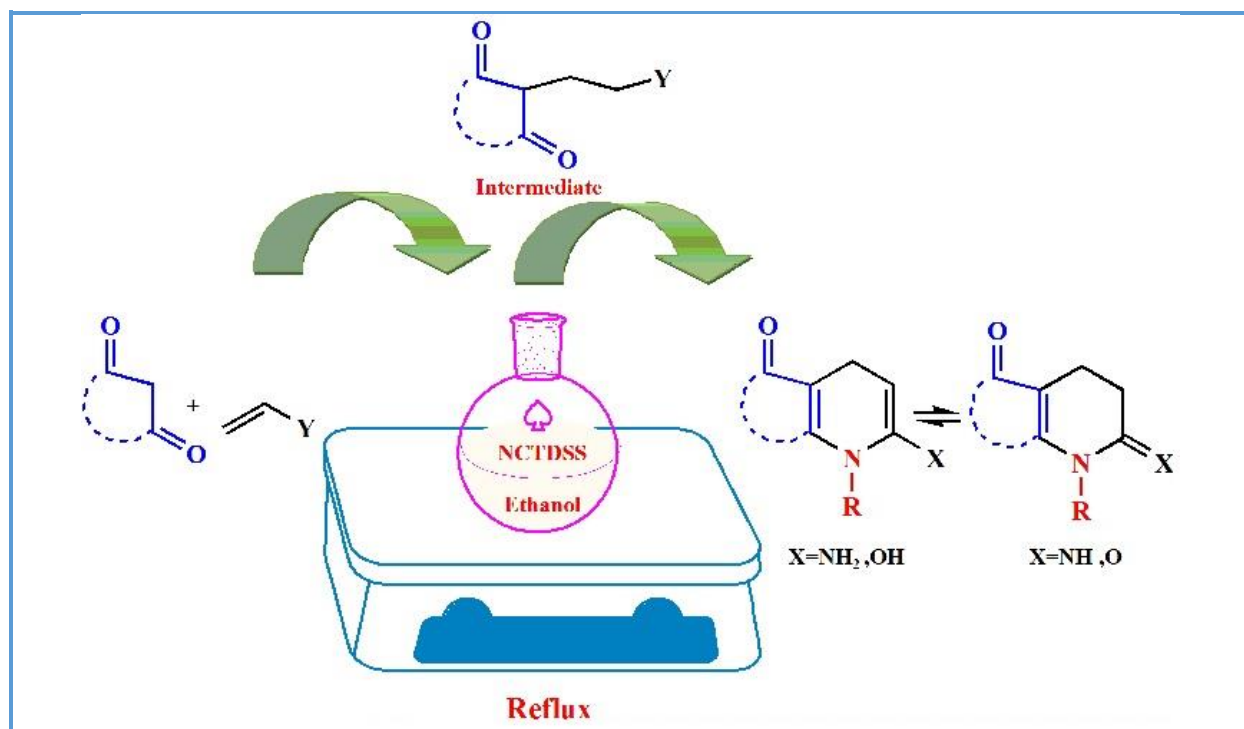
Ethanol

### ABSTRACT

The synthesis of dihydroquinoline derivatives is very important for the pharmaceutical industry due to its many biological activities. In our ongoing efforts to promote new synthetic strategies for preparing heterocyclic compounds in this study, we performed reflux reactions with the nanocrystalline-TiO<sub>2</sub> on dodecyl-sulfated silica support (NCTDSS) catalyst by using a one-pot method. Finally, high-yield products were synthesized and characterized by using different techniques such as FT-IR, <sup>1</sup>H NMR, and <sup>13</sup>C NMR. This procedure has several privileges including simple operation, economy, safe environment, short reaction time, and high-yield.

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## Graphical Abstract



## Introduction

Quinoline is very important for human generation as a heterocyclic structure [1]. Dihydroquinolines and pyridopyrimidines, among quinoline derivatives, are significant structural subunits of natural products that display biological and pharmaceutical activities. The available dihydroquinoline derivatives are multi-functional dihydropyridine derivatives and their chemistry and biology have not been extensively studied in the literature.

Synthetic methods for preparing quinoline derivatives are of notable attention, and various methods have been offered proving desirable results [2–12]. In spite of this, most of them elucidate the synthesis of hydroquinoline nucleus and methods for accessing hydroquinolines with effective functions are scarce in the literature. A number of dihydroquinolines have been synthesized by considering variant biomedical applications

and with the aim of more evaluations of the pharmacological properties of these compounds. Multicomponent reactions (MCRs) are ideal procedures in the synthesis of heterocyclic compounds. The MCRs advantages are simple operation, short reaction time, saving energy, and high yield [13, 14].

In previous studies, various catalysts such as chiral amines, diphenylprolinol trimethylsilyl ether, difunctional thiourea, and tertiary amine-thiourea were used to synthesize dihydroquinoline derivatives [15, 16]. Recently, we offered NCTDSS as an appropriate catalyst for producing organic chromene and coumarin analogs by using a one-pot procedure as a direct route [17]. According to the above results presented, it was predicted that the utilization of the important role represented by the NCTDSS systems, described here and would simplify the expansion of a general and simple one-pot procedure to prepare

dihydroquinolines. On the other hand, nano TiO<sub>2</sub> on silica dodecyl sulfate as a heterogeneous catalyst has advantages such as high effectiveness, reusability, strong oxidation power, easy access, non-toxic, and long-term stability compared with other catalysts.

Only slight modifications of the previously optimized experimental protocol were essential to verify that, in the presence of NCTDSS (5.0 mol %), phenol (1 mmol) and  $\beta$ -ketoesters (1.2 mmol) are smoothly converted into coumarin derivatives in satisfactory yield. Since the optimal conditions for the efficient catalysis of the condensation reaction had been determined. Here, the suitable solvent is ethanol, and it should be emphasized that it is in a clear contrast with the results captured for the dihydroquinolines synthesis. In this research, we aimed to report an efficient sequence for one pot synthesis of dihydroquinoline analogs. Their synthesis was achieved by the one pot reaction of cyclohexylpropanenitrile and cyclohexylpropanoate derivatives with different primary amines in the NCTDSS presence as a catalyst in ethanol at reflux conditions.

## Experimental

### Materials and methods

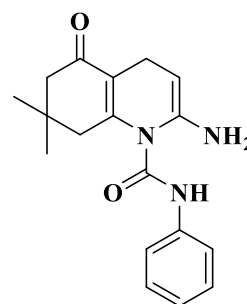
All reagents and starting materials were supplied from Fluka and Aldrich chemical companies and used without more purification. Reaction monitoring was performed by TLC on PolyGram SILG/UV254 silica gel plates. Column chromatography was performed on silica gel columns 60 (mesh 70-230). Melting points in open capillary tubes were characterized in the Barnstead Electro thermal 9100 BZ oil melting point device. <sup>1</sup>H NMR and <sup>13</sup>C NMR spectra were determined by Bruker (250 MHz) Avanc DRX apparatus in pure dutre DMSO-*d*<sub>6</sub> solvent with tetramethyl silane (TMS) as internal standards.

To record mass spectra, FINNIGAN-MAT 8430 mass spectrometer was used operating at 70 eV and FT-IR spectroscopy (Shimadzu FT-IR 8300 spectrophotometer) was operated for recognition.

### General Procedure for synthesis of Dihydroquinolines and Pyridopyrimidines

A mixture of cyclic- $\beta$ -diketone derivatives (1 mmol), acrylonitrile or methyl acrylate (1 mmol) were dissolved in hot ethanol in the presence of 5 mol% of NCTDSS. After appropriate time, primary amine (1 mmol) was added in the mixture, and the resulting mixture was refluxed for fitting time. Reaction progress was assessed by TLC. Upon the reaction completion, the reaction mass was poured into ice-cold water, the product was filtered, washed with water, dried, and recrystallized from hot ethanol, but some compounds which did not reach this level, were purified by column chromatography on silica gel by using hexane/ethyl acetate as eluent to afford the pure dihydroquinolines and pyridopyrimidines.

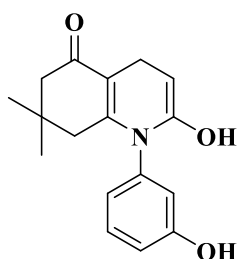
### 2-Amino-5,6,7,8-tetrahydro-7,7-dimethyl-5-oxo-N-phenylquinoline-1(4H)-carboxamide (1)



White solid, mp 165-167 °C, IR (KBr) ( $\nu_{\max}$ / cm<sup>-1</sup>): 3425.3, 3313.5, 3217, 3039.6, 2962.4, 2322.1, 1654.8, 1554.5, 1450.4, 1357.8, 1226.6, 1122.5, 752.2, 698.2, and 586.3. <sup>1</sup>H-NMR (250 MHz, DMSO-*d*<sub>6</sub>):  $\delta$  0.96 (s, 6H), 2.10 (s, 2H), 2.46 (s, 2H), 3.03 (s, 2H), 4.67 (d, *J* = 2.5 Hz, 2H), 5.15 (t, *J* = 2.5 Hz, 1H), 6.88-7.21 (m, 3H), 7.33-7.38 (m, 2H), 8.29 (s, 1H). <sup>13</sup>C-NMR (62.9 MHz,

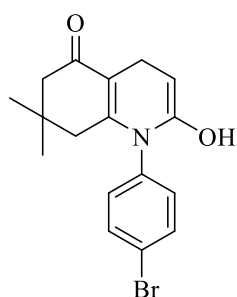
DMSO- $d_6$ ):  $\delta$  19.2, 28.6, 32.2, 42.9, 50.6, 74.2, 116.3, 122.4, 128.2, 130.9, 133.9, 140.7, 146.91, 148.2, 195.3. Anal. Calcd. for  $C_{18}H_{21}N_3O_2$  (311.16): C 69.43; H 6.80; N 13.49, found: C 69.37; H 6.86; N 13.43. MS:  $m/z$  (%) = 311.16 ( $M^+$ ), 246 (33), 215 (36.1), 172 (20.7), 111 (18.5), 83 (38.7), 57 (100).

*7,8-Dihydro-2-hydroxy-1-(3-hydroxyphenyl)-7,7-dimethylquinolin-5(1H,4H,6H)-one (2)*



Yellow solid, mp 188-190 °C, IR (KBr) ( $\nu_{max}/cm^{-1}$ ): 3330, 3004, 2966, 1695, 1510, 1438, 1410, 1255, 1125.5, 1021, 831, 702.2, and 512.9.  $^1H$ -NMR (250 MHz, DMSO- $d_6$ ):  $\delta$  1.08 (s, 6H), 2.02 (s, 2H), 2.24 (s, 2H), 3.87 (d,  $J = 2.5$  Hz, 2H), 4.39 (t,  $J = 5$  Hz, 1H), 5.91 (s, 1H), 6.47-6.58 (m, 3H), 7.08-7.15 (m, 1H), 8.68 (s, 1H).  $^{13}C$ -NMR (62.9 MHz, DMSO- $d_6$ ):  $\delta$  27.6, 32.0, 41.9, 50.2, 63.9, 100.8, 112.3, 120.3, 125.2, 126.3, 135.5, 146.2, 155.6, 179.6, 196.6.

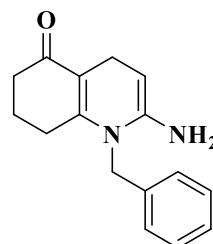
*1-(4-Bromophenyl)-7,8-dihydro-2-hydroxy-7,7-dimethylquinolin-5(1H,4H,6H)-one (3)*



Yellow solid, mp 154-156 °C, IR (KBr) ( $\nu_{max}/cm^{-1}$ ): 3240, 3174, 3043, 2954, 1690, 1523, 1488, 1400, 1280.6, 1149.5, 1072.3, 810, 717.5, and 524.6.  $^1H$ -NMR (250 MHz, DMSO- $d_6$ ):  $\delta$  0.96 (s, 6H), 1.16 (s, 2H), 2.47 (s, 2H), 2.99 (d,  $J = 2.5$  Hz, 2H), 3.5 (s, 1H), 5.26 (t,  $J = 2.5$  Hz, 1H), 7.10-7.14

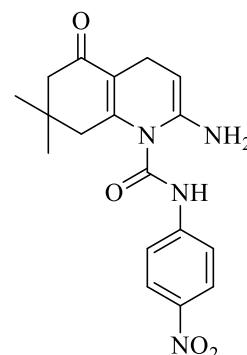
(m, 2H), 7.48-7.53 (m, 2H).  $^{13}C$ -NMR (62.9 MHz, DMSO- $d_6$ ):  $\delta$  17.1, 27.8, 32.2, 41.9, 50.0, 97.3, 111.2, 115.8, 124.5, 131.9, 138.6, 159.3, 181.6, 195.6. Anal. Calcd. for  $C_{17}H_{18}BrNO_2$  (348.23): C 58.63; H 5.21, N 4.02, found: C 58.58; H 5.26; N 3.96. MS:  $m/z$  (%) = 348.23 ( $M^+$ ), 329 (1), 295 (34.2), 239 (59.7), 173 (10.6), 157 (17.1), 130 (32.3), 91 (15.7), 68 (37.8), 57 (100).

*2-Amino-1-benzyl-7,8-dihydroquinolin-5(1H,4H,6H)-one (4)*



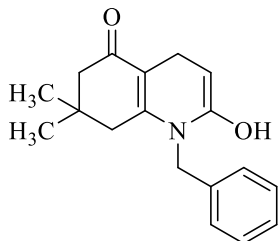
White solid, mp 194.2-196 °C, IR (KBr) ( $\nu_{max}/cm^{-1}$ ): 3475.5, 3244, 3058, 2935.5, 1725, 1558.4, 1454.2, 1377.1, 1203.5, 1072.3, 941.2, and 594.  $^1H$ -NMR (250 MHz, DMSO- $d_6$ ):  $\delta$  1.77-1.82 (m, 4H), 2.48 (m,  $J = 2.5$  Hz, 2H), 3.74 (t,  $J = 2.5$  Hz, 2H), 4.5 (s, 2H), 4.75 (d,  $J = 2.5$  Hz, 2H), 5.46 (t,  $J = 2.5$  Hz, 1H), 7.24-7.50 (m, 5H).  $^{13}C$ -NMR (62.9 MHz, DMSO- $d_6$ ):  $\delta$  20.2, 21.3, 31.4, 43.1, 46.1, 75.2, 107.3, 127.7, 128.1, 128.6, 143.8, 145.1, 170.6, 197.5. Anal. Calcd. for  $C_{16}H_{18}N_2O$  (254.14): C 75.56; H 7.13; N 11.01, found: C 75.50; H 7.18; N 10.54. MS:  $m/z$  (%) = 254.14 ( $M^+$ ), 237 (4.7), 194 (4.2), 152 (3.8), 123 (5.9), 106 (20.1), 79 (50.3), 57 (100).

*1-(4-Nitrophenylamino)-2-amino-7,8-dihydro-7,7-dimethylquinolin-5(1H,4H,6H)-one (5)*



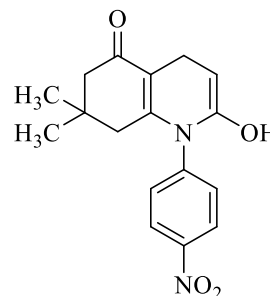
Orange solid, mp 114-116 °C, IR (KBr) ( $\nu_{\max}/\text{cm}^{-1}$ ): 3321.2, 2931.6, 2326, 1715, 1604.7, 1473.5, 1253.6, 1107.1, 1037.6, 837, 748.3, 690.5, and 524.6.  $^1\text{H-NMR}$  (250 MHz,  $\text{DMSO-}d_6$ ):  $\delta$  1.92 (s, 6H), 1.97 (s, 2H), 2.07 (s, 2H), 2.48 (s, 2H), 3.86 (d,  $J = 2.5$  Hz, 2H), 4.46 (t,  $J = 2.5$  Hz, 1H), 7.09 (d,  $J = 10$  Hz, 2H), 8.02 (d,  $J = 10$  Hz, 2H), 9.76 (s, 1H).  $^{13}\text{C-NMR}$  (62.9 MHz,  $\text{DMSO-}d_6$ ):  $\delta$  22.0, 31.2, 34.9, 43.7, 52.4, 94.0, 108.2, 116.4, 125.0, 141.3, 148.5, 150.0, 152.9, 199.8. Anal. Calcd. for  $\text{C}_{17}\text{H}_{20}\text{N}_4\text{O}_3$  (328.15): C 62.18; H 6.14; N 17.06, found: C 62.25; H 6.20; N 17.00.

*1-Benzyl-7,8-dihydro-2-hydroxy-7,7-dimethylquinolin-5(1H, 4H, 6H)-one (6)*



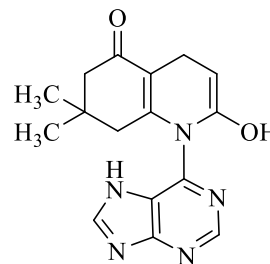
Yellow solid, mp 140-142 °C, IR (KBr) ( $\nu_{\max}/\text{cm}^{-1}$ ): 3440, 3003, 2944, 1705, 1520, 1456, 1301, 1284, 1149.5, 1072.3, 820, 717.4, and 534.6.  $^1\text{H-NMR}$  (250 MHz,  $\text{DMSO-}d_6$ ):  $\delta$  1.31 (s, 6H), 1.88 (s, 2H), 2.46 (s, 2H), 3.34 (s, 1H), 3.35 (s, 2H), 3.37 (d,  $J = 2.5$  Hz, 2H), 5.99 (t,  $J = 2.5$  Hz, 1H), 7.23-7.49 (m, 5H).  $^{13}\text{C-NMR}$  (62.9 MHz,  $\text{DMSO-}d_6$ ):  $\delta$  20.1, 26.9, 28.9, 45.6, 48.3, 50.7, 75.2, 108.0, 128.5, 128.8, 138.7, 141.1, 151.7, 178.2, 184.4. Anal. Calcd. for  $\text{C}_{18}\text{H}_{21}\text{NO}_2$  (283.16): C 76.29; H 7.47; N 4.94, found: C 76.23; H 7.52; N 4.88.

*7,8-Dihydro-2-hydroxy-7,7-dimethyl-1-(4-nitrophenyl)quinolin-5(1H,4H,6H)-one (7)*



Yellow solid, mp 104-106 °C, IR (KBr) ( $\nu_{\max}/\text{cm}^{-1}$ ): 3479.3, 3359.8, 2954.7, 1623.9, 1600, 1442.7, 1307.6, 1222.8, 1110.9, 979.8, 817.8, 752.2, 698.2, and 532.6.  $^1\text{H-NMR}$  (250 MHz,  $\text{DMSO-}d_6$ ):  $\delta$  0.96 (s, 6H), 2.10 (s, 2H), 2.23 (s, 2H), 3.35 (s, 1H), 3.86 (d,  $J = 2.5$  Hz, 2H), 4.99 (t,  $J = 2.5$  Hz, 1H), 6.54-6.61 (m, 2H), 7.89-7.94 (m, 2H).  $^{13}\text{C-NMR}$  (62.9 MHz,  $\text{DMSO-}d_6$ ):  $\delta$  14.9, 27.8, 32.1, 41.9, 50.2, 63.9, 112.3, 120.3, 126.3, 135.5, 146.2, 155.6, 179.6, 196.6. Anal. Calcd. for  $\text{C}_{17}\text{H}_{18}\text{N}_2\text{O}_4$  (314.13): C 64.96; H 5.77; N 8.91, found: C 64.90; H 5.83; N 8.86. MS:  $m/z$  (%) = 314.13 ( $\text{M}^+$ ), 307 (22.5), 249 (16.5), 232 (19.7), 132 (18.1), 105 (10.7), 86 (53.2), 56 (100).

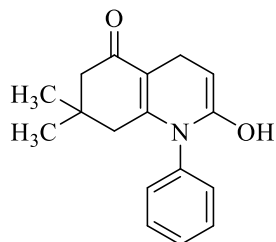
*7,8-Dihydro-2-hydroxy-7,7-dimethyl-1-(7H-purin-6-yl)quinolin-5(1H,4H,6H)-one (8)*



White solid. mp 309 °C (decomposed), IR (KBr) ( $\nu_{\max}/\text{cm}^{-1}$ ): 3571.9, 3136, 2912.3, 2842.6, 1701, 1600.8, 1411.8, 1303.8, 1238.2, 1080.1, 948.9, 717.5, 636.5, and 505.3.  $^1\text{H-NMR}$  (250 MHz,  $\text{DMSO-}d_6$ ):  $\delta$  0.8 (s, 6H), 1.15 (s, 2H), 1.19 (s, 2H), 2.40 (d,  $J = 3$  Hz, 2H), 3.44 (t,  $J = 2.5$  Hz, 1H), 5.50 (s, 1H), 8.06 (s, 1H), 8.28 (s, 1H).  $^{13}\text{C-NMR}$  (62.9 MHz,  $\text{DMSO-}d_6$ ):  $\delta$  22.0, 28.9, 31.2, 56.0, 59.5, 69.3, 116.4, 125.5, 141.3, 148.5, 150.0, 152.9, 170.7, 186.4, 199.8. Anal. Calcd for  $\text{C}_{16}\text{H}_{17}\text{N}_5\text{O}_2$  (311.14): C 61.72; H 5.50; N 22.49, found: C 61.66; H 5.55; N 22.42. MS:  $m/z$  (%) =

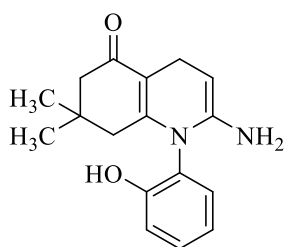
311.14 (M<sup>+</sup>), 246 (19.1), 215 (43.5), 172 (55.7), 131 (15.1), 89 (22.2), 57 (100).

*7,8-Dihydro-2-hydroxy-7,7-dimethyl-1-phenylquinolin-5(1H,4H,6H)-one (9)*



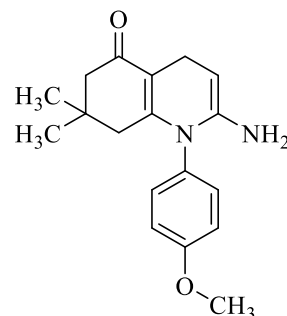
Yellow solid, mp 80-82 °C, IR (KBr) ( $\nu_{\max}/\text{cm}^{-1}$ ): 3340, 3003, 2944, 1732, 1511, 1466, 1371, 1246, 1199, 1072.3, 717.4, and 534.6. <sup>1</sup>H-NMR (250 MHz, CDCl<sub>3</sub>):  $\delta$  1.07 (s, 6H), 1.25 (s, 2H), 1.34 (s, 2H), 2.22 (d,  $J = 2.5$  Hz, 2H), 4.04 (s, 1H), 5.42 (t,  $J = 2.5$  Hz, 1H), 6.68-6.79 (m, 3H), 7.12-7.19 (m, 2H). <sup>13</sup>C-NMR (62.9 MHz, CDCl<sub>3</sub>):  $\delta$  14.1, 29.7, 32.4, 42.9, 50.6, 64.3, 101.4, 115.1, 118.4, 123.9, 129.2, 146.5, 176.5, 199.9. Anal. Calcd. for C<sub>17</sub>H<sub>19</sub>NO<sub>2</sub> (269.14): C 75.81; H 7.11; N 5.20, found: C 75.76; H 7.17; N 5.14.

*2-Amino-7,8-dihydro-1-(2-hydroxyphenyl)-7,7-dimethylquinolin-5(1H,4H,6H)-one (10)*



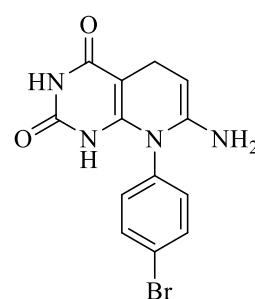
White solid, mp 214-216 °C, IR (KBr) ( $\nu_{\max}/\text{cm}^{-1}$ ): 3232.5, 3066.6, 2950.9, 2727.1, 1700, 1562.2, 1519.8, 1454.2, 1373.2, 1245.9, 1149.5, 813.9, and 767.6. <sup>1</sup>H-NMR (250 MHz, DMSO-*d*<sub>6</sub>):  $\delta$  0.99 (s, 6H), 1.98 (s, 2H), 2.33 (s, 2H), 2.58 (s, 1H), 3.98 (d,  $J = 2.5$  Hz, 2H), 5.44 (t,  $J = 2.5$  Hz, 1H), 6.75-7.07 (m, 4H), 9.61 (s, 1H). <sup>13</sup>C-NMR (62.9 MHz, DMSO-*d*<sub>6</sub>):  $\delta$  16.3, 28.2, 32.6, 41.8, 50.4, 96.3, 116.5, 119.2, 125.9, 127.1, 127.2, 138.1, 142.8, 151.8, 162.3, 194.9. Anal. Calcd for C<sub>17</sub>H<sub>20</sub>N<sub>2</sub>O<sub>2</sub> (284.15): C 71.81; H 7.09; N 9.85, found: C 71.75; H 7.15; N 9.80.

*2-Amino-7,8-dihydro-1-(4-methoxyphenyl)-7,7-dimethylquinolin-5(1H,4H,6H)-one (11)*



Yellow solid, mp 177-179 °C, IR (KBr) ( $\nu_{\max}/\text{cm}^{-1}$ ): 3400, 3205.5, 2831.3, 1690, 1542.9, 1458.1, 1369.4, 1242.1, 1149.5, 1033.8, 806.2, and 563.2. <sup>1</sup>H-NMR (250 MHz, DMSO-*d*<sub>6</sub>):  $\delta$  1.08 (s, 6H), 2.19 (s, 2H), 2.31 (s, 2H), 2.52 (s, 2H), 3.47 (s, 3H), 4.09 (d,  $J = 2.5$  Hz, 2H), 5.37 (t,  $J = 2.5$  Hz, 1H), 6.82-6.86 (m, 2H), 7.04-7.08 (m, 2H). <sup>13</sup>C-NMR (62.9 MHz, DMSO-*d*<sub>6</sub>):  $\delta$  24.9, 27.9, 34.9, 44.1, 52.3, 52.5, 85.4, 110.4, 119.8, 122.4, 133.9, 140.7, 144.7, 194.2. Anal. Calcd. for C<sub>18</sub>H<sub>22</sub>N<sub>2</sub>O<sub>2</sub> (298.17): C 72.46; H 7.43; N 9.39, found: C 72.50; H 7.52; N 9.30.

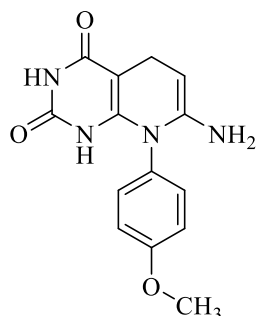
*7-amino-8-(4-bromophenyl)pyrido[2,3-*d*]indole-2,4(1H,3H,5H,8H)-dione (12)*



Yellow solid, mp 245-247 °C, IR (KBr) ( $\nu_{\max}/\text{cm}^{-1}$ ): 3313.2, 3047.3, 2904.6, 1697.2, 1508.2, 1485.1, 1180.2, 813.9, 682.8, 567, and 486. <sup>1</sup>H-NMR (250 MHz, DMSO-*d*<sub>6</sub>):  $\delta$  2.48 (s, 2H), 4.31 (d,  $J = 2.5$  Hz, 2H), 4.74 (t,  $J = 2.5$  Hz, 1H), 7.09-7.17 (m, 2H), 7.46-7.59 (m, 3H), 11.11 (s, 1H). <sup>13</sup>C-NMR (62.9 MHz, DMSO-*d*<sub>6</sub>):  $\delta$  20.7, 89.7, 97.2, 118.0, 123.5, 132.4, 134.4, 137.9, 144.9, 151.6, 167.7. Anal. Calcd. for C<sub>13</sub>H<sub>11</sub>BrN<sub>4</sub>O<sub>2</sub> (334.01): C 46.59; H 3.31; N 16.72, found: C

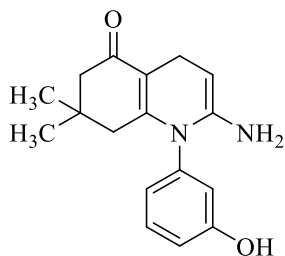
46.53; H 3.37; N 16.68. MS:  $m/z$  (%) = 335.01 ( $M^+$ ), 314 (23.1), 226 (23.1), 172 (16.6), 137 (25.1), 107 (25.5), 83 (53.2), 57 (100).

7-Amino-8-(4-methoxyphenyl)pyrido[2,3-d]pyrimidine-2,4(1H,3H,5H,8H)-dione (13)



Yellow solid, mp 223-225 °C, IR (KBr) ( $\nu_{\max}/\text{cm}^{-1}$ ): 3300.2, 3117.3, 2904.6, 1720, 1528.2, 1325.1, 1180.2, 713.9, 682.8, and 476.  $^1\text{H-NMR}$  (250 MHz,  $\text{DMSO-}d_6$ ):  $\delta$  2.48 (s, 2H), 3.45 (s, 3H), 4.31 (d,  $J = 2.5$  Hz, 2H), 4.74 (t,  $J = 2.5$  Hz, 1H), 7.09-7.66 (m, 5H), 10.69 (s, 1H).  $^{13}\text{C-NMR}$  (62.9 MHz,  $\text{DMSO-}d_6$ ):  $\delta$  22.0, 55.9, 77.4, 81.4, 112.4, 116.4, 125.5, 141.3, 148.5, 150.0, 152.9, 161.3. Anal. Calcd. for  $\text{C}_{14}\text{H}_{14}\text{N}_4\text{O}_3$  (286.11): C 58.73; H 4.93; N 19.57, found: C 58.67; H 4.99; N 19.53.

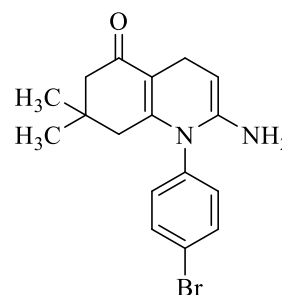
2-Amino-7,8-dihydro-1-(3-hydroxyphenyl)-7,7-dimethylquinolin-5(1H,4H,6H)-one (14)



Pink solid, mp 162-164 °C, IR (KBr) ( $\nu_{\max}/\text{cm}^{-1}$ ): 3224.8, 3058.9, 2962.4, 1568, 1481.2, 1388.7, 1265.2, 1153.4, 991.3, 852.5, and 767.6.  $^1\text{H-NMR}$  (250 MHz,  $\text{DMSO-}d_6$ ):  $\delta$  0.99 (s, 6H), 2.03 (s, 2H), 2.33 (s, 2H), 2.47 (s, 2H), 3.46 (d,  $J = 2.5$  Hz, 2H), 4.75 (t,  $J = 2.5$  Hz, 1H), 6.44-6.60 (m, 3H), 7.1 (t,  $J = 7.5$  Hz, 1H), 9.5 (s, 1H).  $^{13}\text{C-NMR}$  (62.9 MHz,  $\text{DMSO-}d_6$ ):  $\delta$  19.0, 33.1, 37.4, 47.2, 55.2, 93.1, 102.1, 109.0, 114.7, 116.6, 118.6,

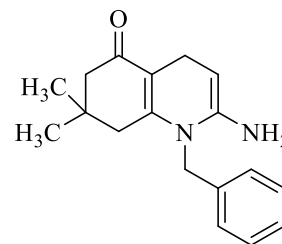
135.0, 145.3, 163.1, 165.3, 200.7. Anal. Calcd. for  $\text{C}_{17}\text{H}_{20}\text{N}_2\text{O}_2$  (284.35): C 71.81; H 7.09; N 9.85, found: C 71.75; H 7.14; N 9.79. MS:  $m/z$  (%) = 284.35 ( $M^+$ ), 232 (33.8), 216 (28.1), 175 (38.3), 133 (42.1), 109 (18.1), 83 (18), 57 (100).

2-Amino-1-(4-bromophenyl)-7,8-dihydro-7,7-dimethylquinolin-5(1H,4H,6H)-one (15)



Light green solid, mp 190-192 °C, IR (KBr) ( $\nu_{\max}/\text{cm}^{-1}$ ): 3213.2, 3039.6, 2869.9, 1589.2, 1538.4, 1485.1, 1404.1, 1245.9, 1122.5, 1006.8, 813.9, 682.8, 567, and 486.  $^1\text{H-NMR}$  (250 MHz,  $\text{DMSO-}d_6$ ):  $\delta$  1.00 (s, 6H), 2.18 (s, 2H), 2.24 (s, 2H), 2.37 (s, 2H), 4.15 (d,  $J = 2.5$  Hz, 2H), 5.17 (t,  $J = 2.5$  Hz, 1H), 7.06-7.20 (m, 2H), 7.45-7.60 (m, 2H).  $^{13}\text{C-NMR}$  (62.9 MHz,  $\text{DMSO-}d_6$ ):  $\delta$  17.0, 27.7, 32.2, 41.9, 50.0, 97.2, 111.2, 115.8, 124.5, 131.9, 138.6, 159.1, 159.3, 195.6. Anal. Calcd. for  $\text{C}_{17}\text{H}_{19}\text{BrN}_2\text{O}$  (347.25): C 58.80; H 5.52; N 8.07, found: C 58.85; H 5.60; N 8.11. MS:  $m/z$  (%) = 347.25 ( $M^+$ ), 295 (38.8), 239 (49), 210 (11), 172 (60.3), 130 (39.5), 107 (40.5), 91 (53), 68 (55), 57 (100).

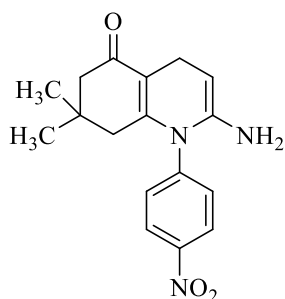
2-Amino-1-benzyl-7,8-dihydro-7,7-dimethylquinolin-5(1H,4H,6H)-one (16)



White solid, mp 259-261 °C, IR (KBr) ( $\nu_{\max}/\text{cm}^{-1}$ ): 3440, 3178.2, 2935.5, 1720.3, 1533, 1265.2, 1391.8, 1300, 1257.5, 1153.4, 1080.1, 971, and

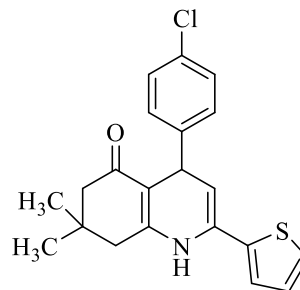
850.  $^1\text{H-NMR}$  (250 MHz,  $\text{DMSO-}d_6$ ):  $\delta$  0.96 (s, 6H), 2.47 (s, 2H), 2.48 (s, 2H), 3.25 (s, 2H), 4.22 (d,  $J = 2.5$  Hz, 2H), 5.22 (t,  $J = 2.5$  Hz, 1H), 5.5 (s, 2H), 7.21-7.55 (m, 5H).  $^{13}\text{C-NMR}$  (62.9 MHz,  $\text{DMSO-}d_6$ ):  $\delta$  14.5, 26.8, 32.0, 41.9, 42.7, 46.2, 84.5, 117.5, 127.4, 127.5, 128.2, 134.4, 136.4, 158.4, 184.4. Anal. Calcd. for  $\text{C}_{18}\text{H}_{22}\text{N}_2\text{O}$  (282.17): C 76.56; H 7.85; N 9.92, found: C 76.50; H 7.89; N 9.87.

*2-Amino-7,8-dihydro-7,7-dimethyl-1-(4-nitrophenyl)quinolin-5(1H,4H,6H)-one (17)*



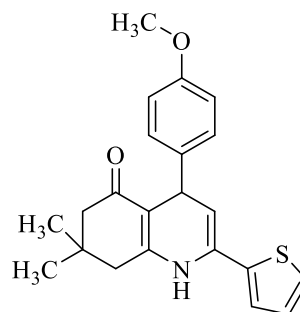
Yellow solid, mp 228-230 °C, IR (KBr) ( $\nu_{\text{max}}$ /  $\text{cm}^{-1}$ ): 3380.3, 3190.5, 3078.2, 2935.5, 1690.2, 1523.7, 1492.8, 1346.2, 1257.5, 1153.4, 1080.1, 979.8, and 894.9.  $^1\text{H-NMR}$  (250 MHz,  $\text{DMSO-}d_6$ ):  $\delta$  1.02 (s, 6H), 2.15 (s, 2H), 2.45 (s, 2H), 2.98 (s, 2H), 3.52 (d,  $J = 2.5$  Hz, 2H), 5.56 (t,  $J = 2.5$  Hz, 1H), 7.36 (d,  $J = 7.5$  Hz, 2H), 8.26 (d,  $J = 7.5$  Hz, 2H).  $^{13}\text{C-NMR}$  (62.9 MHz,  $\text{DMSO-}d_6$ ):  $\delta$  18.4, 27.6, 32.3, 41.9, 49.1, 100.3, 112.3, 120.9, 124.8, 142.1, 145.6, 156.9, 159.7, 195.9. Anal. Calcd. for  $\text{C}_{17}\text{H}_{19}\text{N}_3\text{O}_3$  (313.25): C 65.16; H 6.11; N 13.41, found: C 65.10; H 6.18; N 13.36. MS:  $m/z$  (%) = 313.25 ( $\text{M}^+$ ), 236 (19.7), 147 (10.2), 129 (13.6), 109 (22.1), 83 (51.4), 57 (100).

*4-(4-Chlorophenyl)-7,8-dihydro-7,7-dimethyl-2-(thiophen-2-yl)quinolin-5(1H,4H,6H)-one (18)*



Yellow solid, mp 213-215 °C, IR (KBr) ( $\nu_{\text{max}}$ /  $\text{cm}^{-1}$ ): 3277, 3028, 2924, 2874, 1681, 1647, 1581, 1487, 1444, 1406, and 1300.  $^1\text{H-NMR}$  (250 MHz,  $\text{DMSO-}d_6$ ):  $\delta$  1.08 (s, 3H), 1.10 (s, 3H), 2.05-2.21 (m, 2H), 2.39 (s, 2H), 4.59-4.61 (d, 1H), 5.21-5.23 (d, 1H), 6.92-6.94 (d,  $J = 8.6$  Hz, 2H), 7.23-7.25 (d,  $J = 8.08$  Hz, 2H), 7.00-7.02 (m, 1H), 7.13-7.17 (m, 1H), 7.33-7.34 (m, 1H), 8.40 (s, 1H).

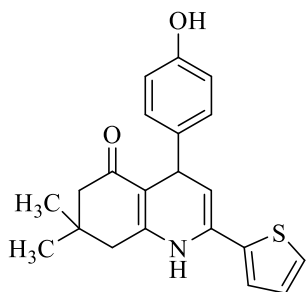
*7,8-Dihydro-4-(4-methoxyphenyl)-7,7-dimethyl-2-(thiophen-2-yl)quinolin-5(1H,4H,6H)-one (19)*



Yellow solid, mp 190-192 °C, IR (KBr) ( $\nu_{\text{max}}$ /  $\text{cm}^{-1}$ ): 3255, 3061, 2955, 1653, 1577, 1498, 1477, and 1388.  $^1\text{H-NMR}$  (250 MHz,  $\text{DMSO-}d_6$ ):  $\delta$  1.0 (s, 3H), 1.08 (s, 3H), 2.04-2.21 (m, 2H), 2.47 (s, 2H), 3.75 (s, 1H), 4.52-4.53 (d, 1H), 5.21-5.23 (d, 1H), 6.76-6.78 (d,  $J = 7.92$  Hz, 2H), 7.23-7.25 (d,  $J = 8.56$  Hz, 2H), 7.00-7.02 (m, 1H), 7.15-7.17 (m, 1H), 7.33-7.34 (t, 1H), 8.42 (s, 1H).

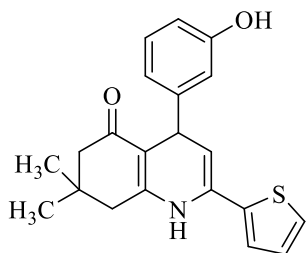
*7,8-Dihydro-4-(4-hydroxyphenyl)-7,7-dimethyl-2-(thiophen-2-yl)quinolin-5(1H,4H,6H)-one (20)*





Yellow solid, mp 208-210 °C, Lit. mp 212-214 °C.

7,8-dihydro-4-(3-hydroxyphenyl)-7,7-dimethyl-2-(thiophen-2-yl)quinolin-5(1H,4H,6H)-one (21)

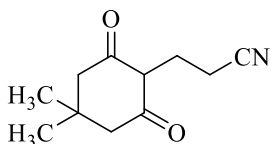


Yellow solid, mp 207-209 °C, Lit. mp 203-205 °C.

General procedure for Michael addition reaction using NCTDSS as catalyst

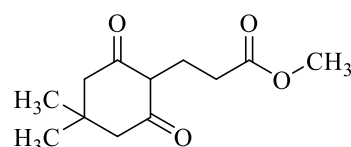
A mixture of Michael-donors (1 mmol), activated olefins (1.5 mmol) and NCTDSS (0.05 g, 5 mol%) in ethanol was kept at 78 °C in an oil bath for the stipulated time. The progress of the reaction was monitored by TLC. After the reaction completion, the mixture was washed with ethyl acetate (10 mL) and the crude product was obtained after removing ethyl acetate from the washing solution. Further purification was carried out by recrystallization from ethyl acetate/petroleum ether or short column chromatography on silica gel (ethyl acetate/petroleum ether).

3-(4,4-Dimethyl-2,6-dioxocyclohexyl)propanenitrile (22)



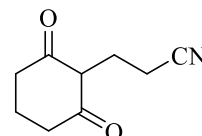
Oil, IR (KBr) ( $\nu_{\max}$ /  $\text{cm}^{-1}$ ): 2962.4, 1731.9, 1461.9, 1357.8, 1222.8, 1145.6, 1654.8, 1037.6, 871.8, 829.3, and 597.9.  $^1\text{H-NMR}$  (250 MHz,  $\text{CDCl}_3$ ):  $\delta$  1.00 (s, 6H), 1.14-1.32 (m, 2H), 2.13 (s, 2H), 2.20 (s, 2H), 3.82 (q, 2H), 4.11 (t,  $J = 7.5$  Hz, 1H).  $^{13}\text{C-NMR}$  (62.9 MHz,  $\text{CDCl}_3$ ):  $\delta$  14.0, 22.6, 28.2, 32.4, 50.6, 64.1, 121.3, 199.5. MS:  $m/z$  (%) = 193.2 ( $\text{M}^+$ ), 185 (2.6), 149 (35.1), 129 (15.4), 97 (26.3), 73 (51.3), 57 (100).

Methyl 3-(4,4-dimethyl-2,6-dioxocyclohexyl)propanoate (23)



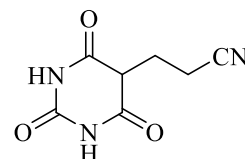
Oil, IR (KBr) ( $\nu_{\max}$ /  $\text{cm}^{-1}$ ): 2962.4, 2873.7, 2341.4, 1651, 1489.7, 1222.8, 1145.6, 1033.8, 852.5, 632.6, 613.3, and 420.5.  $^1\text{H-NMR}$  (250 MHz,  $\text{CDCl}_3$ ):  $\delta$  1.13 (s, 6H), 1.40 (t,  $J = 5$  Hz, 2H), 2.27 (s, 2H), 2.33 (s, 2H), 3.87-3.98 (m, 2H), 4.03 (t,  $J = 7.5$  Hz, 1H), 4.24 (s, 3H).  $^{13}\text{C-NMR}$  (62.9 MHz,  $\text{CDCl}_3$ ):  $\delta$  14.0, 28.2, 32.4, 42.8, 50.6, 64.1, 101.4, 176.1, 199.5. MS:  $m/z$  (%) = 226.3 ( $\text{M}^+$ ), 166 (17.8), 149 (52.7), 123 (15.4), 85 (27.5), 57 (100).

3-(2,6-Dioxocyclohexyl)propanenitrile (24)



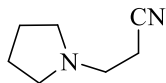
Oil, IR (KBr) ( $\nu_{\max}$ /  $\text{cm}^{-1}$ ): 2900, 2850.1, 1710, 1621, 1489.1, 1149.5, and 1011.9. MS:  $m/z$  (%) = 165.2 ( $\text{M}^+$ ), 143 (100), 115 (37.1), 87 (24.9), 55 (38.8).

3-(Hexahydro-2,4,6-trioxopyrimidin-5-yl)propanenitrile (25)



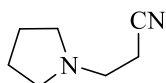
Viscous Oil, IR (KBr) ( $\nu_{\max}/\text{cm}^{-1}$ ): 3350, 2910, 2870.1, 1720, 1650, 1559.1, 1229.5, and 1101.9.

3-(Pyrrolidin-1-yl)propanenitrile (26)



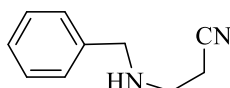
Oil,  $^1\text{H-NMR}$  (250 MHz,  $\text{CDCl}_3$ ):  $\delta$  1.10 (m, 4H), 2.55 (m, 2H), 2.65 (m, 2H), 2.70 (m, 4H) [18].

3-(Diethylamino)propanenitrile (27)



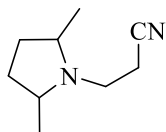
Oil.  $^1\text{H-NMR}$  (250 MHz,  $\text{CDCl}_3$ ):  $\delta$  1.70 (m, 6H), 2.55 (m, 2H), 2.71 (m, 6H).

3-(Benzylamino)propanenitrile (28)



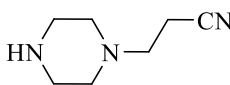
Oil,  $^1\text{H-NMR}$  (250 MHz,  $\text{CDCl}_3$ ):  $\delta$  2.52 (t,  $J = 2.2$  Hz, 2H), 2.83 (t,  $J = 2.2$  Hz, 2H), 3.83 (s, 2H), 7.26-7.34 (m, 5H).

3-(Diisopropylamino)propanenitrile (29)



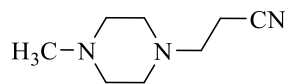
Oil,  $^1\text{H-NMR}$  (250 MHz,  $\text{CDCl}_3$ ):  $\delta$  2.30-2.75 (m, 4H), 3.8 (s, 2H), 7.2-7.4 (m, 5H).

3-(Piperazin-1-yl)propanenitrile (30)



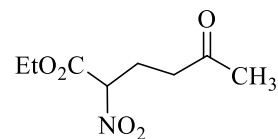
Oil, IR (KBr) ( $\nu_{\max}/\text{cm}^{-1}$ ): 3401, 2850.1, 1619, 1479.1, 1249.5, and 1211.9 [19].

3-(4-Methylpiperazin-1-yl)propanenitrile (31)



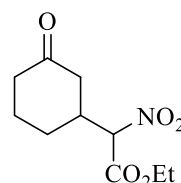
White solid, mp 90-92 °C,  $^1\text{H-NMR}$  (250 MHz,  $\text{CDCl}_3$ ):  $\delta$  2.26 (t,  $J = 2.7$  Hz, 3H), 2.48 (t,  $J = 2.2$  Hz, 8H), 2.67 (s, 2H), 8.22 (s, 1H).

Ethyl-2-nitro-5-oxohexanoate (32)



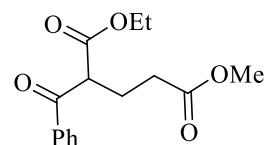
Oil,  $^1\text{H-NMR}$  (250 MHz,  $\text{CDCl}_3$ ):  $\delta$  1.25 (t,  $J = 5$ , 3H), 2.07 (s, 3H), 2.30-2.39 (m, 2H), 2.53-2.59 (m, 2H), 4.16-4.28 (m, 2H), 5.18 (t,  $J = 7.5$  Hz, 1H).  $^{13}\text{C-NMR}$  (62.9 MHz,  $\text{CDCl}_3$ ):  $\delta$  13.6, 24.1, 29.6, 38.4, 63.0, 86.7, 164.3, 206.1.

Ethyl-2-nitro-2-(3-oxocyclohexyl)acetate (33)



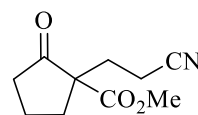
Oil,  $^1\text{H-NMR}$  (250 MHz,  $\text{CDCl}_3$ ):  $\delta$  1.27 (t,  $J = 2.5$  Hz, 3H), 1.81-2.42 (m, 9H), 4.20-5.01 (m, 2H), 6.08 (d,  $J = 2.5$  Hz, 1H).  $^{13}\text{C-NMR}$  (62.9 MHz,  $\text{CDCl}_3$ ):  $\delta$  13.6, 24.1, 29.6, 38.4, 63.0, 86.7, 164.3, 206.1.

1-Ethyl-5-methyl-2-(phenylcarbonyl)pentanedioate (34)



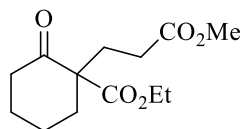
Oil, IR (KBr) ( $\nu_{\max}/\text{cm}^{-1}$ ): 3010, 2881, 1720.3, 1329.1, 1233.5, and 1211.9 [20].

Methyl 1-(2-cyanoethyl)-2-oxocyclopentanecarboxylate (35)



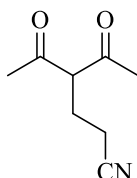
Oil, IR (KBr) ( $\nu_{\max}/\text{cm}^{-1}$ ): 2950.1, 2825, 1629, 1429, 1241.2, and 1213.2.

Ethyl 1-(2-(methoxycarbonyl)ethyl)-2-oxocyclopentanecarboxylate (36)



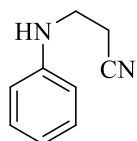
Oil, IR (KBr) ( $\nu_{\max}$ /  $\text{cm}^{-1}$ ): 3005.5, 2850.1, 1699.1, 1523.3, 1441.4, and 1256.7.

#### 4-Acetyl-5-oxohexanenitrile (37)



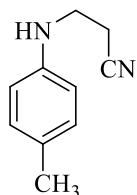
Oil, MS:  $m/z$  (%) = 153.2 ( $M^+$ ), 105 (68.2), 87 (100), 57 (70.8).

#### 3-(Phenylamino)propanenitrile (38)



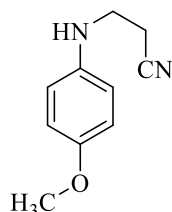
Viscous oil,  $^1\text{H-NMR}$  (250 MHz,  $\text{CDCl}_3$ ):  $\delta$  2.57 (t,  $J = 2.2$  Hz, 2H), 3.46 (dd,  $J = 2.0$  Hz,  $J = 1.9$  Hz, 2H), 3.99 (s, 1H), 6.58-7.22 (m, 5H) [21].

#### 3-(*p*-Toluidino)propanenitrile (39)



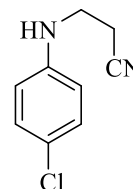
Yellow solid, mp 100-102 °C,  $^1\text{H-NMR}$  (250MHz,  $\text{CDCl}_3$ ):  $\delta$  2.25 (s, 3H), 2.63 (t,  $J = 2.1$  Hz, 2H), 3.51 (t, 2H,  $J = 2.1$  Hz), 3.84 (s, 1H), 6.56 (d,  $J = 2.8$  Hz, 2H), 7.03 (d,  $J = 2.7$  Hz, 2H).

#### 3-(4-Methoxyphenylamino)propanenitrile (40)



Viscous oil,  $^1\text{H-NMR}$  (250 MHz,  $\text{CDCl}_3$ ):  $\delta$  2.52 (t,  $J = 2.2$  Hz, 4H), 3.59 (t,  $J = 2.2$  Hz, 4H), 3.79 (s, 3H), 6.81-6.91 (m, 5H).

#### 3-(4-Chlorophenylamino)propanenitrile (41)

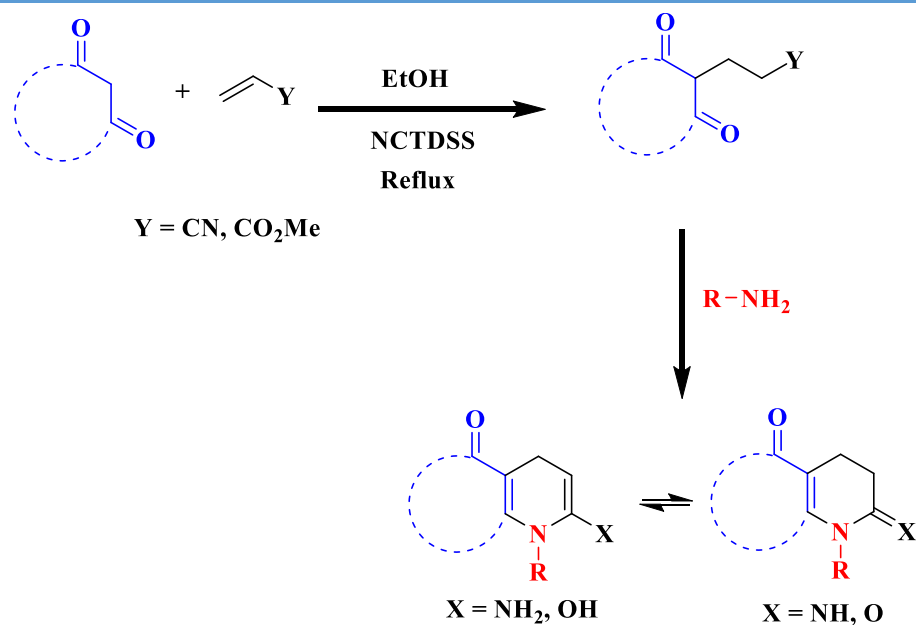


Viscous oil,  $^1\text{H-NMR}$  (250MHz,  $\text{CDCl}_3$ ):  $\delta$  2.64 (t,  $J = 2.2$  Hz, 2H), 3.50 (t,  $J = 2.2$  Hz, 2H), 4.00 (s, 1H), 6.53-7.18 (m, 5H).

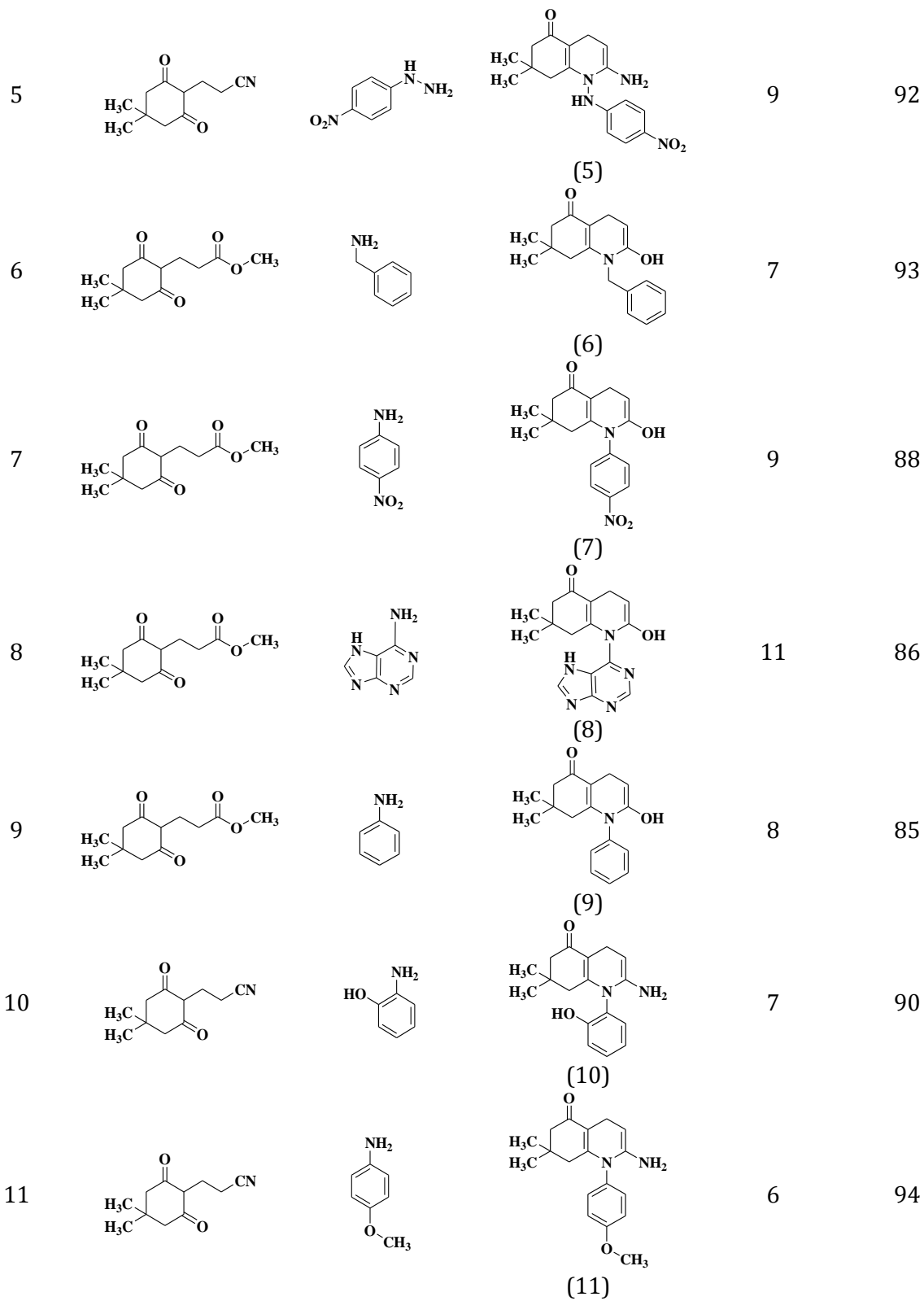
## Results and Discussion

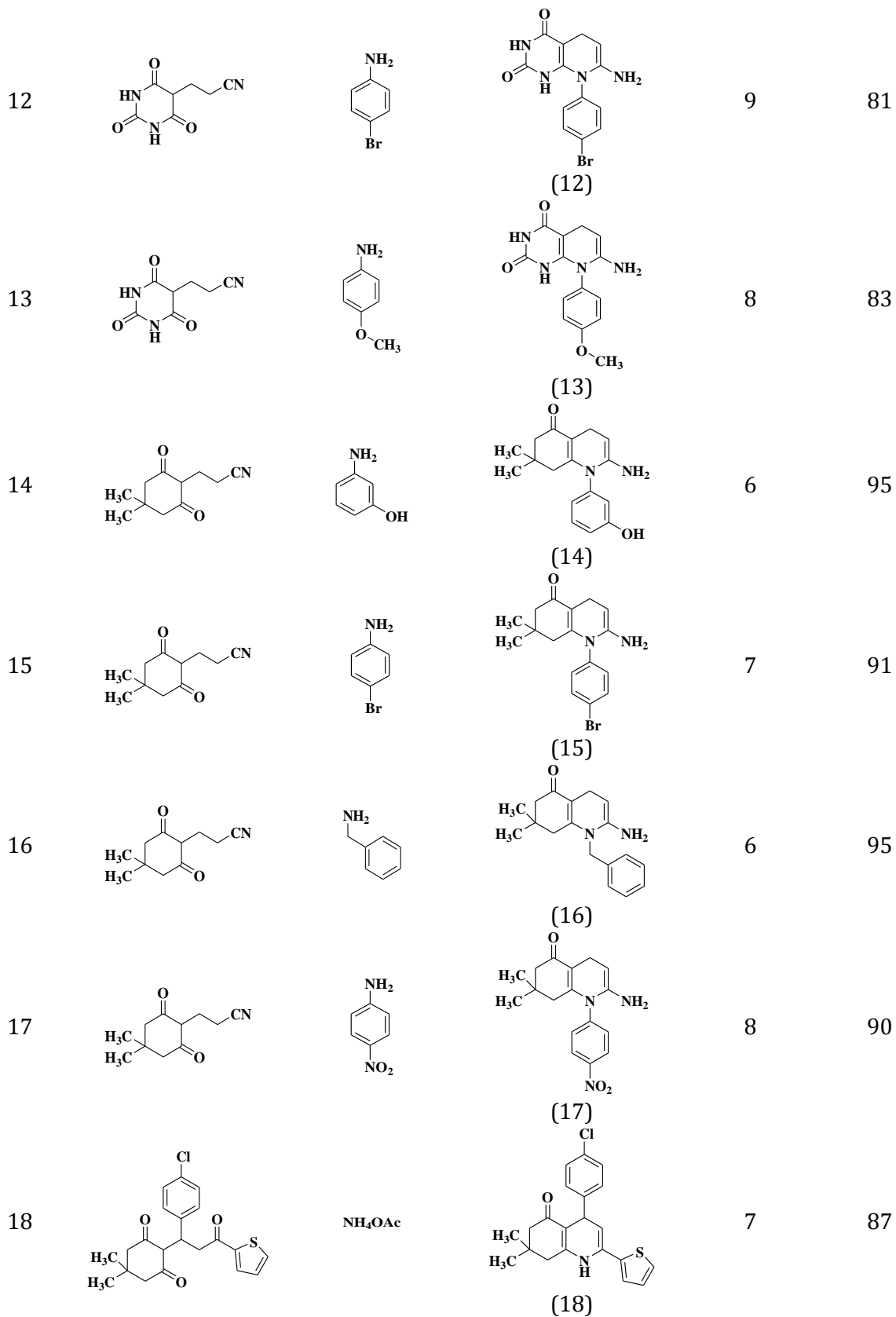
In our initial study, barbituric acid and acrylonitril were dissolved in hot ethanol and in the presence of 5 mol% of NCTDSS. After 20 min, the primary amines were added to the mixture refluxed for fitting time. The corresponding compounds were obtained as a white solid with 81, 83% isolated yield (Table 1, entries 12, 13).

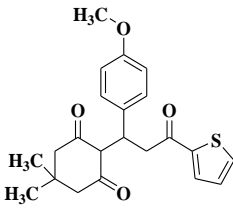
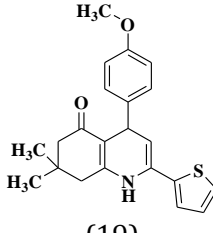
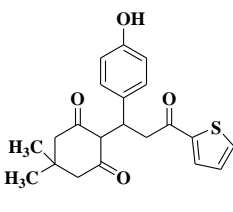
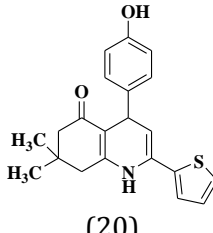
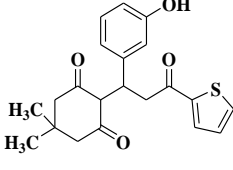
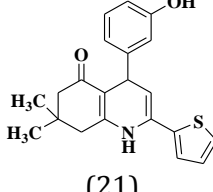
Under the above conditions, the reaction of 3-(4,4-dimethyl-2,6-dioxocyclohexyl)propanenitrile and primary amines were yielded the corresponding hydroquinoline products with 89, 92, 90, 94, 95, 91, 95 and 90% isolated yield, respectively (Table 1, entries 1, 5, 10, 11, 14-17). To further expand our strategy, a new functionalized hydroquinolines was synthesized based on our recent procedure, as represented in Table 1. Since antiviral drugs based on quinolines almost contain a hydroxy and ether chain, we decided to synthesize a category of heterocyclic quinolines. To determine the scope of this protocol, various hydroquinoline derivatives were synthesized under the normalized conditions, and the results are summarized in Table 1.

**Table 1.** Products of one-pot condensation reaction to synthesize dihydroquinolines in the NCTDSS presence as catalyst under reflux conditions

Entry	Substrate	Amine	Product	Time (h)	Yield(%) <sup>b</sup>
1				10	89
2				7	95
3				9	90
4				8	90





19		NH <sub>4</sub> OAc		12	86
20		NH <sub>4</sub> OAc		10	85
21		NH <sub>4</sub> OAc		11	84

<sup>a</sup>catalyst (5 mol% NCTDSS), EtOH (5 mL), and reflux

<sup>b</sup>All yields are isolated

The syntheses of twenty-one compounds occupy a special position among systems containing dihydroquinoline and dihydropyridine rings due to their wide spectrum biological activities.

As listed in Table 1, the generality of this protocol was highlighted by using amines with both electron withdrawing and electron donating groups under the same reaction conditions. Also, we synthesized these products by both aliphatic and aromatic amines in good yields. According to Table 1, for all entries, the reactions were performed in almost same reaction time and the products were obtained with ranging from 81-95% isolated yields. Likewise, cyclohexadione acted as same as dimedone in the designed condensation reaction and the corresponding products were generated with excellent yield (Table 1, entry 4). The structural diversity of this reaction was further increased by using as amine component, leading to the formation of new nucleoside derivative with hydroquinoline moiety (Table 1,

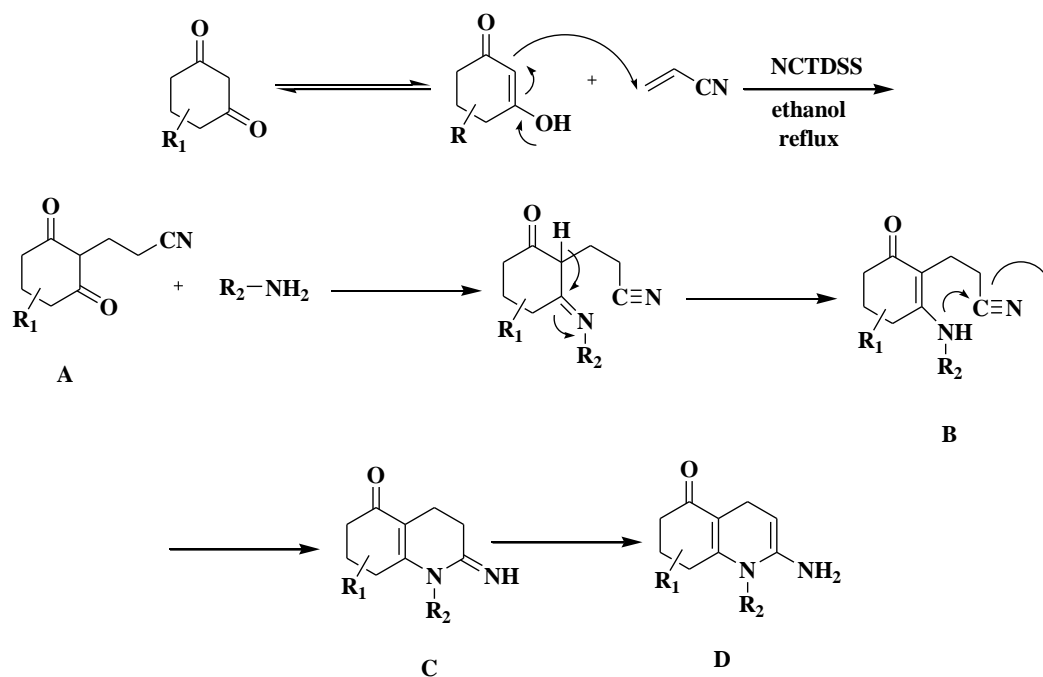
entry 8). According to the Table 1, in all cases, the reactions were accomplished in relatively short reaction time and products were obtained with good to excellent yields (more than 81%).

The proposed mechanism involves Michael addition reaction of 5,5-dimethyl-1,3-cyclohexanedione (dimedone) reacted with acrylonitrile to give the addition product **A**. Then, the intermediate upon condensation with primary amines, afford the intermediate **B**. Cyclization takes place by the nucleophilic attack of amine (NH<sub>2</sub>) group on the CN group to give the intermediate **C**, which loses hydrogen to give the dihydroquinolines **D** followed by intramolecular cyclization and aromatization (Scheme 1).

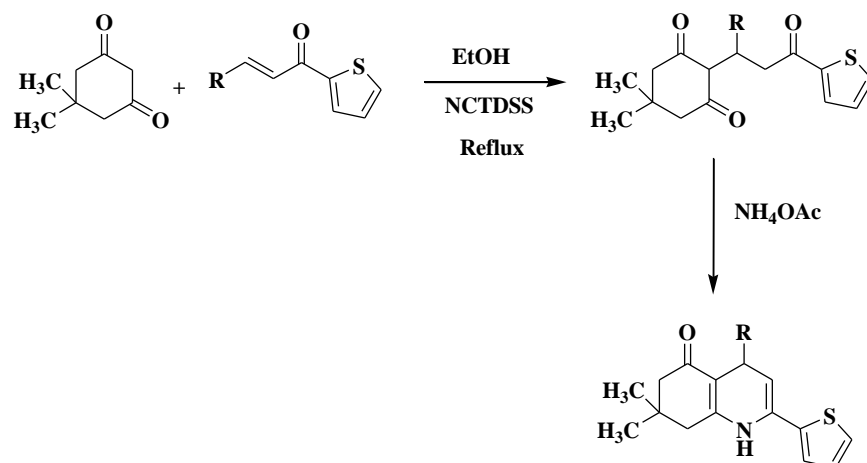
### Mechanism

The synthesis of entries 18-21 were achieved by reflux assisted one pot reaction of 5,5-dimethylcyclohexane-1,3-dione (dimedone) with 3-phenyl-1 (thiophen-2-yl)

pop-2-en-1-one derivatives, respectively in the presence of excess amounts of ammonium acetate (Scheme 2).



**Scheme 1.** Michael addition reaction for the synthesis of dihydroquinolines derivative



**Scheme 2.** Synthesis of dihydroquinoline derivatives in the presence of ammonium acetate

To sum up, this research describes an efficient one pot access to a new class of heterocyclic dihydroquinoline analogs having quinoline or pyrimidine-fused ring in their structural frameworks. To obtain these

categories of heterocyclic compounds, amine component incorporate in the structure of obtained molecule by a C-N linkage. This protocol is general for a wide range of amines and carbonyl compounds. The biological



activity of some synthesized compounds is under assessment and will be report in future.

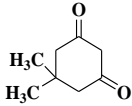

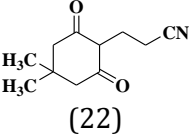
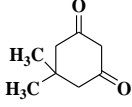
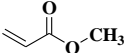
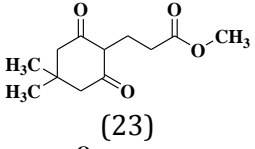
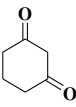

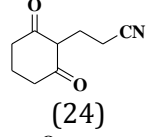
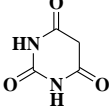

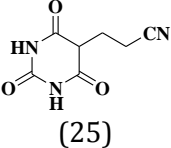


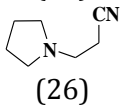


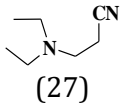
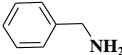

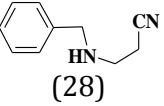


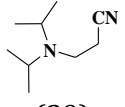


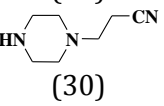
In another part of this study, we also synthesized Michael addition products by using different donors and acceptors. These products were synthesized by NCTDSS as a catalyst to obtain compounds **1-21**.

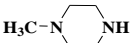

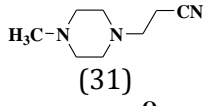
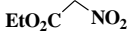
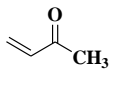
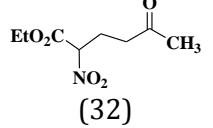
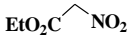

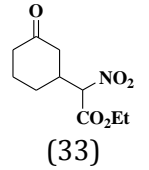
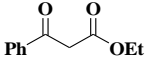
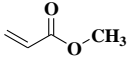
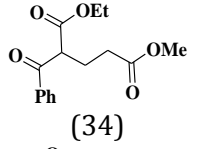
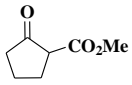

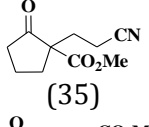
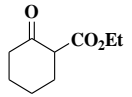
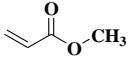
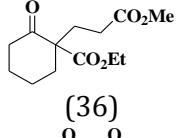


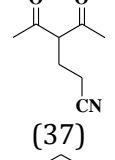


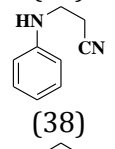
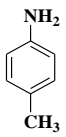

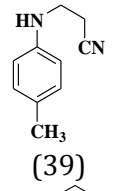
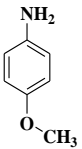

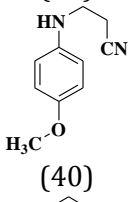
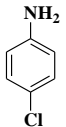

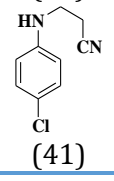
The Michael addition is widely identified as one of the most substantial bond-forming reactions in organic synthesis [20]. This type of reaction is generally administrated by using strong base metal reagents in organic solvents

such as THF, DMF, and DMSO under dry conditions [19].

To affirm the feasibility of our catalyst design concept, we prepared a variety of products, starting from commercially available cyclohexadiones and amino derivatives with different functional groups. Then, the catalytic (NCTDSS) studies of the Michael addition reaction were performed in ethanol at the reflux conditions. The results are summarized in [Table 2](#).

**Table 2.** Michael addition reaction<sup>a</sup>

Entry	Donor	Acceptor	Product	Time (min)	Yield (%) <sup>b</sup>
1			 (22)	10	97
2			 (23)	10	97
3			 (24)	15	92
4			 (25)	20	85
5			 (26)	19	90
6			 (27)	22	82
7			 (28)	21	91
8			 (29)	24	80
9			 (30)	26	86

10			 (31)	26	87
11			 (32)	25	84
12			 (33)	25	95
13			 (34)	35	90
14			 (35)	35	92
15			 (36)	33	92
16			 (37)	33	92
17			 (38)	30	91
18			 (39)	28	93
19			 (40)	26	96
20			 (41)	34	87

<sup>a</sup>Reactions carried out at reflux condition, using donor (1 mmol), acceptor (1.5 mmol), and catalyst (5 mol %) in EtOH (5 mL)

<sup>b</sup>Isolated yield

## Conclusions

Our protocol avoids utilizing expensive reagents and high temperatures, and the catalyst can be recovered. Additional applications are currently under investigation [22]. A variety of structurally diverse  $\alpha,\beta$ -unsaturated carbonyl compounds underwent Michael additions smoothly in the NCTDSS presence to generate the corresponding compounds in good yields. Generally, the reactivity decreased with electron withdrawing groups of donor (Table 2) and electron donating groups of acceptor. Apart from acrylonitrile, methyl acrylate, but-3-en-2-one and cyclohex-2-enone can be further the substrates of this reaction to afford the desired products in good yields and in short reaction times. Dimedone showed higher reactivity than barbituric acid. Diisopropyl amine revealed rather lower reactivity because of the strong steric hindrance. The ethyl 3-oxo-3-phenylpropanoate examined underwent Michael addition with methyl acrylate favorably and corresponding product could be obtained in good yields in much more slowly reaction times. In addition, five-membered *N*-heterocycles exhibited a high reactivity (Table 2).

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## Authors' contributions

All authors contributed to data analysis, drafting, and revising of the paper and agreed to be responsible for all the aspects of this work.

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